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Methicillin sensitive staphylococcus aureus screening and decolonisation in elective hip and knee arthroplasty

Edward Jeans[a,*], Richard Holleyman[a], David Tate[b], Mike Reed[a], Ajay Malviya[a]

[a] Northumbria Healthcare NHS Foundation Trust, Department of Trauma and Orthopaedics, Wansbeck General Hospital, Woodhorn Lane, NE63 9JJ, UK
[b] Northumbria Healthcare NHS Foundation Trust, Department of Microbiology, Wansbeck General Hospital, Woodhorn Lane, NE63 9JJ, UK

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SUMMARY

Aims: Periprosthetic joint infection (PJI) is a catastrophic and potentially life threatening complication following arthroplasty. In addition to the resulting impact on patient morbidity and mortality, PJI is associated with significant financial cost, which is estimated at £21,937 per case. Methicillin sensitive staphylococcus aureus (MSSA) is a common isolate in PJI and colonisation is a proven risk factor for subsequent infection. The aims of this study were: (1) to determine if MSSA screening and decolonisation reduced MSSA PJI rate in primary joint replacement and (2) to determine cost effectiveness of such a screening program.

Methods: Pre-operative screening for MSSA was introduced in our institution in 2010. All MSSA positive patients attending for elective arthroplasty were prescribed Octenisan body wash and nasal Bactroban for use 5 days prior to procedure, and five days after. Infection data was collected prospectively and compared with a control group from before.

Results: Between 2007 and 2014, 12,910 primary arthroplasties (5917 hip, 6993 knee) were performed. There were 3593 in the pre-screening group and 9318 in the post-screening group. Pre-screening PJI MSSA rate was 0.75% which reduced to 0.25% post screening introduction ($p < 0.0001$). Overall PJI rate fell from 1.92% to 1.41% ($p = 0.03$). The screening program was most effective in MSSA prevention in total hip arthroplasty (3% to 1.5%, $p = 0.002$) and significant in the multivariate analysis. Following the introduction of the screening programme 47 PJIs were avoided, with a cost per infection prevented of £1893.

Conclusion: The MSSA screening and eradication protocol used in our institution was effective at reducing rates of MSSA PJI. Furthermore, it resulted in significant savings when compared to the cost of prevented infections.

Introduction

The number of joint replacements performed is increasing year on year with an aging population.[1,2] This is in addition to hemi-arthroplasty implants used for treating elderly patients with a hip fracture. Periprosthetic joint infection (PJI) is a serious and potentially life threatening complication.[3] According to the 12th annual national joint registry (NJR) report[4] the revision burden for infection stands at 1332 (14% of total revisions) per annum for Hip arthroplasty and 1417 (23%) for Knee arthroplasty. A large proportion of patients have debridement and retention of a prosthesis; that is not included in the NJR and therefore the true implication of PJI on the health service is much worse. This burden is increasing and similar across different health care systems.[5] With revision surgery having higher morbidity and mortality than a primary procedure every effort should be made to minimize PJI.[6] There is also a cost burden associated with treatment of infection and this can be anywhere between £15,000– £20,000, with costs escalating for revision procedure and recently estimated to be as much as £21,937 per revision in British practice.[7–9] The solution is almost always further aggressive surgery or lengthy courses of antibiotics to suppress the infection, or both. Despite current treatments, the relative survival rate of patients with PJI is 87.3% at five years. For comparison, the five-year relative survival rates for the top five most common cancers are 99% for prostate cancer, 89% for breast cancer, 17% for lung and bronchial cancer, 65% for colorectal cancer, and 92% for melanoma.[10]

Staphylococcus species are a common isolate in PJI[11] with Methicillin Sensitive Staphylococcus Aureus (MSSA) being the predominant pathogen isolated in 24.6% and Methicillin Resistant Staphylococcus Aureus (MRSA) 3.3% in England.[12] Between 25–30% of the United Kingdom population is positive for skin or nasal carriage of Staphylococcus, with MSSA prevalence estimated

* Corresponding author.
E-mail address: edward.jeans@nhs.net (E. Jeans).

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Table 1
Demographics and risk factors.

	2007–2009 ($n=3593$)	2010–2014 ($n=9318$)	p value
Gender % (M:F)	**46/54**	**45/55**	**0.1**
Mean age (range)	68.5 (22–100)	68.6 (16–99)	0.571
Mean BMI (range)	**29.5 (17.3–50.2)**	**29.9 (15.6–61)**	**0.009**
Mean length of stay (range)	5.61 (0–59)	3.85 (0–64)	<0.0001

at 20%.[13–15] Colonisation is a proven risk factor for subsequently developing surgical site infection during hospital stay with isolates matching those of nasal swabs in 85% of cases, suggesting that the majority of PJI are endogenous.[16–18] Decolonisation would therefore be expected to have a positive impact in reducing PJI. MRSA screening and decolonisation is well attested in the literature to be effective at reducing infection rates.[14,15,17] Evidence is emerging that screening programme for MRSA and MSSA may lead to a reduction in Staphylococcus infection rate.[19] In a double blind placebo controlled multi center trial of surgical patients decolonised with mupirocin and chlorhexidine verses placebo, the rate of MSSA SSI was lower in the treatment group (3.4% v 7.7%, relative risk of infection 0.42), although total SSIs were not reported.[20] Other studies have shown that mupirocin is effective at reducing nasal colonisation and that cost saving can be made by screening.[20–22]

The study aims to determine if MSSA screening and decolonisation programme can reduced MSSA PJI rates in primary joint replacement. A secondary aim is to determine cost effectiveness of such screening programme.

Methods

In 2010 our institution adopted a pre operative screening and decolonisation programme for carriers of MSSA in elective joint replacement along with standard mandatory MRSA screening. Prior to the introduction of screening there was no set protocol for MSSA screening and eradication, while MRSA testing and decolonisation was performed across the whole study period. The screening programme consists of swab collection for MRSA and MSSA. Nasal and groin swabs are taken at pre operative screening by a trained practitioner and the method of collection and site (nose and groin) did not vary between the pre and post MSSA screening groups. The swabs were processed in the microbiology laboratory on Colorex *Staphylococcus aureus* media (E & O Laboratories Ltd, England) plates were read between 18 and 24 h pink colonies went on for further identification using the VITEK MS (MALDI –TOF, Biomerieux, France) and sensitivity testing using the VITEK 2 (Biomerieux, France). The clinical team was alerted to all positive swabs. All patients attending for elective arthroplasty are given Octenisan bodywash (Ocetenidin, Schülke & Mayr UK Ltd, Sheffield, UK) to use for 5 days prior to surgery. Those found to be MSSA positive are additionally given Bactroban (Mupirocin, Glaxo-SmithKline UK Limited, Brentford, UK) to be applied to both nostrils four times per day for 5 days prior to the procedure and for 5 days after. No further swabs were taken to confirm eradication on admission.

Northumbria Healthcare NHS Foundation Trust performs arthroplasty surgery in three hospitals with the surgical team operating across the different locations. The make up of the surgical team and implants used did not significantly change throughout the study period. A single infection surveillance team monitors infection rates for all cases and gathers data centrally. Data from Public Health England surgical site infection surveillance service was crossed referenced with this centrally gathered data. Public Health England's published standard on superficial, deep and organ space infection identified those hip and knee arthroplasties that had been complicated by PJI.[23] The use of this standard remained constant during the study period. Data obtained for procedure performed, age, gender, body mass index (BMI), American society of anaesthesiologist (ASA) physical status, duration of surgery, length of hospital stay (LOS), causative organism and sensitivities. Infection monitoring has been performed with complete data available from prior to screening programme (1st January 2007 to 31st December 2009) and after its introduction (1st January 2010 to 31st August 2014). This study is a retrospective review of this prospectively collected data.

Table 2
Pre and post screening ASA grade.

ASA	2007–2009 (n)	%	2010–2014 (n)	%
1	**332**	**12.3**	**1193**	**13.2**
2	1933	71.3	6549	72.3
3	**437**	**16.1**	**1269**	**14.0**
4	8	0.3	42	0.5

Statistical analysis was performed using STATA (StataCorp. 2013. *Stata Statistical Software: Release 13*. College Station, TX: StataCorp LP) all results quoted to three significant figures. Categorical data was analysis using $\chi 2$ test, continuous by an independent samples T-test. Significant variables were then used to build a logistic regression model. For those PJI with multiple organisms, if any of the cultured organisms included MSSA then they were included in the MSSA group for analysis.

Results

There were 12,911 hip and knee arthroplasties performed during the study period, with 3593 in the pre-screening group and 9318 in the post-screening group.

Demographics

Details of demographics and risk factors for PJI are presented in Tables 1 and 2. The duration of length of stay decreased significantly after 2010. The BMI was slightly higher in the study group (t-test, $p=0.009$) and also the ASA status of the two groups was significantly different (Chi squared $p=0.02$).

Infection rate

In the pre screening group 69 (1.92%) PJI were identified while in the post screening group it was 131 (1.41%) ($p=0.03$). Table 3 shows the change in infection rate with a significant decrease in the MSSA infection rate ($p<0.0001$), while the non-MSSA infection rate remained the same during the study period. This effect was predominantly in the hip replacement group.

In the pre-screening group of the 69 PJI, 15 (21.7%) cultured multiple organisms (range 2 and 3); while of the 131 PJI in the post-screening group, 30 (22.9%) were multi organism (range 2 and 3).

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Table 3
Pre and post screening infections by organism and operation type.

	Prescreening group (2007–2010)			Post screening group (2010–2014)			
	Number	Infection	%	Number	Infection	%	*p* value
Total	**3593**	**69**	**1.92**	**9318**	**131**	**1.41**	**0.03**
MSSA		28	0.75		23	0.25	<0.0001
Non MSSA		**41**	**1.17**		**108**	**1.16**	**0.93**
TKR	1969	21	1.07	5024	67	1.33	0.37
MSSA		**9**	**0.40**		**13**	**0.26**	**0.18**
Non MSSA	12	0.67			54	1.07	0.07
THR	**1624**	**48**	**2.96**	**4293**	**64**	**1.49**	**0.0002**
MSSA		19	1.17		10	0.23	<0.0001
Non MSSA		**29**	**1.79**		**54**	**1.26**	**0.12**

Regression analysis

A multivariate logistic regression model for predictors of MSSA PJI (including deep and superficial infection) was constructed. The significant variables were LOS (coefficient = 0.095, 95%CI 0.060 to 0.131, $p < 0.001$), BMI (coefficient = 0.100, 95%CI 0.044 to 0.156, $p < 0.001$) and MSSA screening programme (odds ratio = 0.407, 95%CI 0.190 to 0.873, $p = 0.02$). The multivariate model for overall infection (deep and superficial infection with any organism) showed that the significant predictors were LOS (coefficient = 0.102, 95%CI 0.078 to 0.126, $p < 0.001$), BMI (coefficient = 0.090, 95%CI 0.062 to 0.118, $p < 0.001$) and hip replacement (odds ratio = 1.66, 95%CI 1.165 to 2.365, $p = 0.005$).

Cost analysis

The average cost of screening is £8 per patient with a total cost of £74,544 (9318 patients). Approximately 20% of these patients would be MSSA positive (20,26), the cost of treating these would be (including postage of Octenisan and Bactroban) £7.73 per patient with a total cost of £14,409 (1864 patients). The total cost implication of the screening programme has therefore been £88,953.

If the MSSA infection rate remained at 0.75% during the post-screening period, the number of possible MSSA infection would be expected to be 70 instead of 23 that was noted in the post surveillance group. Therefore the screening programme prevented a possible 47 patients from having MSSA infection. Thus the average cost of avoiding each infection can be estimated to be £1893 (£88,953/47).

Discussion

In a cohort of 12,911 patients over the study period where data was prospectively collected we have found a significant decrease in the MSSA infection rate after the introduction of the screening program, with an additional decrease in the overall infection rate from 1.9% to 1.4% ($p = 0.03$). This decrease was predominantly in the hip replacement group (3% to 1.5%, $p = 0.002$). We have estimated it to be at a cost saving of £1893 per expected infection.

MRSA screening and decolonising has been universally adopted in England by government mandate and has demonstrated a decrease in MRSA surgical site infection rate.[24] Decolonisation is low cost via nasal mupirocin (Bactroban) ointment and an octenidine (Octenisan) shower on the day of or day before surgery being the recommendation. Despite the focus on MRSA, S. aureus species remain a common cause of prosthetic joint infection, almost always being MSSA. After the introduction of the MSSA decolonisation programme we have noted a three-fold reduction in the MSSA infection rate from 0.75% to 0.25% ($p < 0.0001$). In 2010 Bode et al[20] showed that identification of S. aureus nasal carriers by means of a rtPCR assay, followed by decolonising patients who were carriers of MSSA resulted in reduced rates of surgical site infection. The inclusion criterion for screening was the expectation that a patient would remain hospitalised for at least four days in one of the participating departments (internal medicine, cardiothoracic surgery, vascular surgery, orthopedics, gastrointestinal surgery, or general surgery). Across the whole cohort of patients they reported that the rate of S. aureus infection in carriers was 3.4% (17 of 504) in the decolonised group compared to 7.7% (32 of 413) in the placebo group. This was a significant reduction ($p = 0.008$) with a relative risk of infection, 0.42 (95% confidence interval (CI), 0.23–0.75) in the decolonised group. The study, however, only included 135 orthopaedic patients of whom 95 had hip or knee replacement. We have demonstrated the benefit of this programme in a much larger group of orthopaedic patients (12,911) undergoing primary joint replacement. MSSA screening does remain a contentious issue and the most recent international consensus statement of PJI chose to not recommend universal decolonisation of all patients by a majority of 85%.[24] A review of the literature published in the same year shows Level II–IV evidence for decolonisation from 19 studies[25] along with MRSA screening and decolonisation is now included in WHO guidelines.[26]

The screening programme does add to the overall cost of the preoperative optimization process, but the economic burden of PJI counters this. In the cost benefit analyses that we have performed this has come at a cost of £1893 per S. aureus infection prevented. Financial analyses of revision arthroplasty have revealed the mean cost per septic revision in the UK is £21,937.[9] We have therefore been able to save a substantial amount over the study period with an estimated total cost benefit of £1,031,039 ($21{,}937 \times 47$) in terms of reduction of costs of managing these infections. Subsequent to the 2010 publication by Bode et al, a subgroup analyses was performed by the authors[22] which showed that the decolonised orthopaedic patients cost €955 less than non-treated patients ($n = 135$, €6097 vs €7052, $p = 0.05$). As is apparent there is potential for large amount of cost saving, if this is accepted through the NHS.

PJI infection is complex and multifactorial. In multivariable logistical regression modelling hospital length of stay, BMI and having a hip operation all emerged as significant independent predictors for all infections. While multivariate analysis showed that MSSA screening programme was a significant factor in preventing MSSA infection, a univariate analysis was shown to significantly reduce overall infection rate ($p = 0.03$). A number of strategies have been implemented at our institution with the aim of reducing length of stay following primary arthroplasty which has fallen significantly in recent years. It is therefore difficult to conclude whether length of stay was a true risk factor for the development of PJI when also modelling for MSSA screening which was is itself defined according to two time periods. We did note that the

knee replacement cohort did not have a proportionate benefit from the screening programme with no change in overall infection rate (1.07% vs 1.33%, $p = 0.37$) or MSSA infection rate (0.40% vs 0.26%; $p = 0.18$). This is difficult to explain, we have not come across anything in the literature to prove why MSSA screening and decolonisation would be more effective in hips than in knees.

Understandably in an age of concern over antibiotic resistance the wide spread use of antibiotics pre operatively must be evidence based. In the population undergoing arthroplasty surgery topical antibiotics are used for short defined lengths and it is unlikely in this setting that a person will be exposed to multiple courses in a short period of time limiting the risk of selecting for resistant organisms. PJI is often treated with prolonged courses of antibiotics and an effective screening programme may be of benefit in preventing antibiotic resistance, but re-colonisation and resistance have proven to be a problem in institutions seeking to eradicate MRSA.[27] The raise is community acquired resistant S. Aureus infections also supports our selective use of decolonization, rather than universal treatment. Our microbiology department routinely monitors MSSA sensitivities and has not reported a significant rise in resistance to mupirocin, since the introduction of this screening and treatment protocol. In our institution the current protocol does not include the routine rescreening of patients on admission for elective joint surgery following decolonisation. This decision was taken as MSSA positive patients would have had 5 days of treatment pre admission and protocolled to continue with nasal treatment for 5 days following surgery therefore repeat screening would have only added costs to the screening program without changing the management of the patient. It has however been shown in previous work that the protocol used in our institution is effective in reducing the carriage rates of MSSA.[28] Whether some of these patients continued to be positive for MSSA despite treatment is unknown and of course whether this contributed to some MSSA infection in the post screening programme cohort is difficult to exclude or confirm.

Demographic data was obtained from our submissions to the National Joint Registry. Between the two groups there was a significant change in compliance with data entry for example BMI entry went from 44.2% in the prescreening group to 83.2% in the post screening group. A key limitation of our study was that the groups were not randomised and improvement in infection rates could have been down to other factors. However, a sufficiently powered randomised control trial to demonstrate a 0.5% difference (as we report) in PJI would require 3000 patients in each arm. The dramatic reduction in MSSA SSI ($p < 0.0001$) compared to the non MSSA SSI ($p = 0.93$) suggests that screening and decolonisation was responsible. Another limitation was that we have not reported on the number of patients who were positive for MSSA carriage during the study period. However, we have clearly noted the benefit of this “intention to treat” screening programme with a significant reduction in MSSA positive infection and the overall infection rate in this group of patients undergoing primary joint replacement. The cost-benefit analyses demonstrates the potential saving that we have made over the study period in economic terms not withstanding the benefits in terms of social, emotional and personal suffering.

In conclusion this study represents the largest case series in the literature so far detailing the effects off MSSA screening and decolonisation. We have shown a significant improvement in both MSSA following the introduction of screening and that significant cost savings have resulted from the programme.

Conflict of Interest

No conflict of interest to declare.

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None of the study authors have received any financial inducement in relation to the preparation of this manuscript. As the corresponding author, I can confirm I have had full access to the data relating to this manuscript and take responsibility for its accuracy and publication

Ethics approval

Local ethics approval received for use and publication of data

Authors contributions

Edward Jeans: Data collection, literature review, data analysis and manuscript preparation

Richard Hollymann: Data analysis and interpretation

David Tait: Data interpretation and microbiology advise

Mike Reed: Study design, literature search and data interpretation

Ajay Malviya: Senior author, study design, manuscript preparation and data interpretation

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